

2014 HYPERTENSION  
GUIDELINES

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### Learning Objectives

- Describe specific blood pressure thresholds at which antihypertensive therapy should be initiated and blood pressure goals for specific populations
- Discuss treatment of hypertension: evidence-based dosing, management algorithm, preferred medication classes
- Analyze the 2014 Hypertension Guidelines and compare the recommendations to other treatment guidelines

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### Patient Case

- Mr. C is 66-years-old, referred for hypertension
- Medical history:
  - Idiopathic peripheral neuropathy
  - Hyperglycemia
  - Benign hypertrophy of prostate
  - Gastroesophageal reflux disease
  - Hypertension
  - Anxiety
  - Osteoarthritis
  - Bladder cancer
  - Nephrectomy

- Allergies:
  - Atenolol (hypotension)
  - Citalopram
  - Clonazepam
  - Gemfibrozil
  - Hctz 25 mg
  - Terazosin (insomnia, disorientation)
- Vitals:
  - BP 156/88 mmHg, repeat BP 143/81 mmHg
  - HR 63
  - Wt 234 lb (106.1 kg)
  - BMI 34.63
  - Home BP 140/82 mmHg

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### Patient Case

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**Medications:**

- Flunisolide 0.025% nasal spray- 2 sprays/nostril bid
- Hydrocodone 5 mg/APAP 325 po tid prn pain
- Lorazepam 1 mg po tid prn anxiety
- Metformin 500 mg po bid

**OTC/Herbals:**

- Beta-sitosterol 150 mg po daily
- Calcium/vitamin D po bid
- Fish oil 1 gram po daily
- Vitamin C

**HTN Medications:**

- Amlodipine 10 mg po daily
- Clonidine 0.1 mg po at bedtime
- Lisinopril 40 mg po daily

**Previous HTN Medications:**

- Atenolol
- Enalapril
- Felodipine
- Furosemide
- Hydrochlorothiazide
- Quinopril
- Terazosin

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### Patient Case

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**Relevant Labs (9/25/13):**

- SCr 1.01 mg/dL
- Na+ 140 mEq/L
- K+ 4.0 mEq/L
- Cl- 105 mEq/L
- A1c 5.6%
- 24-hour urine creatinine 1.96 g/24 hr
- 24-hour urine microalbumin 13 mg/24 hr

**What is Mr. C's goal BP?**

- A. < 150/90 mmHg
- B. < 140/90 mmHg
- C. < 140/80 mmHg
- D. < 130/80 mmHg

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### Prevalence of Hypertension in the US

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**Men**

Age, years	Non-Hispanic White	Non-Hispanic Black	Mexican American
18-29	~10%	~15%	~12%
30-39	~15%	~25%	~18%
40-49	~25%	~40%	~30%
50-59	~35%	~55%	~45%
60-69	~45%	~65%	~55%

**Women**

Age, years	Non-Hispanic White	Non-Hispanic Black	Mexican American
18-29	~5%	~10%	~8%
30-39	~10%	~20%	~15%
40-49	~20%	~35%	~25%
50-59	~30%	~50%	~40%
60-69	~40%	~60%	~50%

Prevalence of hypertension in men (upper graph) and women (lower graph) according to age and race/ethnicity in the United States from the NHANES survey. Hypertension occurs earlier and more frequently in non-Hispanic blacks.

From Finkelstein DM, Chou Y, Amini BK. JAMA 2010; 303:2045.

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### Complications of Hypertension

- Cardiovascular disease (CVD)
- Heart failure
- Left ventricular hypertrophy
- Ischemic stroke
- Intracerebral hemorrhage
- Chronic kidney disease (CKD) and end-stage renal disease

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### Causes of Secondary Hypertension

- Obstructive sleep apnea
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Pheochromocytoma
- Coarctation of the aorta
- Cushing's syndrome
- Thyroid or parathyroid disease
- Medications

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### Lifestyle Modifications

Modification	Recommendation	Approximate Systolic BP Reduction
Weight reduction	Maintain normal body weight (BMI 18.5-24.9)	5-20 mmHg/10 kg weight loss
Adoption of DASH eating plan	Consume a diet rich in fruits, vegetables, low-fat dairy products	5-14 mmHg
Dietary sodium restriction	Reduce dietary sodium intake to no more than 2.4 grams/day	2-8 mmHg
Physical activity	Engage in moderate-to-vigorous intensity physical activity for ~160 minutes/week	4-9 mmHg
Moderation of alcohol consumption	Limit alcohol to no more than 2 drinks/day in men and no more than 1 drink/day in women	2-4 mmHg

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### Three Key Questions

- 1. Does initiating antihypertensive therapy at specific BP thresholds improve health outcomes?
- 2. Does treatment with antihypertensive therapy to a specified BP goal lead to improved health outcomes?
- 3. Do various antihypertensive medications or classes differ with respect to health outcomes?

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### Evidence Review

- Adults aged 18 or older with hypertension
- Randomized controlled trials from January 1, 1966 through December 31, 2009
- Effects of the studied intervention on important health outcomes:
  - Overall mortality, CVD-related mortality, CKD-related mortality
  - Myocardial infarction, heart failure, hospitalization for heart failure, stroke
  - Coronary revascularization, other revascularization
  - End-stage renal disease (ESRD), doubling of creatinine, halving of glomerular filtration rate (GFR)

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### Evidence Review

- For trials January 2010 to August 2013
  - Major study in hypertension
  - At least 2000 participants
  - Multi-centered
  - All other exclusion/inclusion criteria met

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## Evidence Review

Type of Evidence	Quality Rating <sup>a</sup>
Well-designed, well-executed RCTs that adequately represent populations to which the results are applied and directly assess effects on health outcomes Well-conducted meta-analyses of such studies Highly certain about the estimate of effect; further research is unlikely to change our confidence in the estimate of effect	High
RCTs with minor limitations affecting confidence in, or applicability of, the results Well-designed, well-executed non-randomized controlled studies and well-designed, well-executed observational studies Well-conducted meta-analyses of such studies Moderately certain about the estimate of effect; further research may have an impact on our confidence in the estimate of effect and may change the estimate	Moderate
RCTs with major limitations Non-randomized controlled studies and observational studies with major limitations affecting confidence in, or applicability of, the results Uncontrolled clinical observations without an appropriate comparison group (eg, case series, case reports) Physiological studies in humans Meta-analyses of such studies Low certainty about the estimate of effect; further research is likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate	Low

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## Evidence Review

Grade	Strength of Recommendation
A	<b>Strong Recommendation</b> There is high certainty based on evidence that the net benefit <sup>a</sup> is substantial.
B	<b>Moderate Recommendation</b> There is moderate certainty based on evidence that the net benefit is moderate to substantial or there is high certainty that the net benefit is moderate.
C	<b>Weak Recommendation</b> There is at least moderate certainty based on evidence that there is a small net benefit.
D	<b>Recommendation against</b> There is at least moderate certainty based on evidence that it has no net benefit or that risks/harms outweigh benefits.
E	<b>Expert Opinion</b> ("There is insufficient evidence or evidence is unclear or conflicting, but this is what the committee recommends.") Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, but the committee thought it was important to provide clinical guidance and make a recommendation; further research is recommended in this area.
N	<b>No Recommendation for or against</b> ("There is insufficient evidence or evidence is unclear or conflicting.") Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, and the committee thought no recommendation should be made. Further research is recommended in this area.

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## Recommendation 1

"In the general population aged 60 years or older, initiate pharmacologic treatment to lower BP at systolic blood pressure (SBP) of 150 mmHg or higher or diastolic blood pressure (DBP) of 90 mmHg or higher and treat to a goal SBP lower than 150 mmHg and goal DBP lower than 90 mmHg."

**Strong Recommendation – Grade A**

**Corollary Recommendation**

"In the general population aged 60 years or older, if pharmacologic treatment for high BP results in lower achieved BP (less than 140 mmHg) and treatment is not associated with adverse effects on health or quality of life, treatment does not need to be adjusted."

**Expert Opinion – Grade E**

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### Age 60 or Older

- Antihypertensive therapy to lower SBP less than 150 mmHg reduces cerebrovascular morbidity and mortality, fatal and nonfatal heart failure, coronary heart disease
- HYVET:
  - Randomized, multi-center, controlled trial
  - 3845 patients who were 80 years or older and SBP greater than 160 mmHg
  - Received indapamide or placebo, and perindopril or placebo if necessary, to achieve target BP 150/80 mmHg
  - Primary end point: fatal or nonfatal stroke

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### Age 60 or Older

- HYVET Results:
  - Active treatment:
    - 30% reduction in rate of fatal or nonfatal stroke (95% CI, -1-51%, P=0.06)
    - 39% reduction in rate of death from stroke (95% CI, 1-62%, P=0.05)
    - 21% reduction in rate of death from any cause (95% CI, 4-35%, P=0.02)
    - 64% reduction in rate of heart failure (95% CI, 42-78%, P<0.001)

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### Age 65 or Older

- No additional benefit of goal SBP lower than 140 mmHg compared with SBP goal of 140-160 mmHg or 140-149 mmHg
- JATOS AND VALISH Trials
- Low quality evidence:
  - Duration of follow-up was not long enough (2 years and 2.85 years)
  - Concerns regarding generalizability of results

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### The Minority View

- Reduction in intensity of antihypertensive treatment in a large population at high risk for CVD
- Insufficient evidence to support increasing the SBP target
- Possible reversal of decades-long decline in CVD, especially stroke mortality
- RCT data not reviewed by panel strongly support SBP goal of less than 140 mmHg
- Conflict with other guidelines
- SBP goal of less than 150 mmHg for frail persons older than 80

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### Recommendation 2

“In the general population younger than 60 years, initiate pharmacologic treatment to lower BP at DBP of 90 mmHg or higher and treat to a goal DBP of lower than 90 mmHg.”

*For ages 30-59 years, Strong Recommendation – Grade A*

*For ages 18-29 years, Expert Opinion – Grade E*

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### Diastolic Blood Pressure

- Initiating antihypertensive therapy in adults 30 years or older with DBP  $\geq$  90 mmHg reduces cerebrovascular morbidity and mortality
  - HDFP: 35% reduction in fatal and non-fatal stroke (P<0.01)
  - MRC: 45% reduction in fatal and non-fatal strokes
- In the general population with hypertension, treatment with antihypertensive therapy to a DBP goal less than 90 mmHg reduces cerebrovascular morbidity and mortality

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## Diastolic Blood Pressure

- Initiating antihypertensive therapy in adults 30 years or older with DBP  $\geq$  90 mmHg reduces overall mortality
  - HDFP: 1.3% absolute decrease in mortality at 5 years (P<0.01)
- Initiating antihypertensive therapy in adults 30 years or older with DBP  $\geq$  90 mmHg reduces heart failure

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## Diastolic Blood Pressure – HOT Trial

- HOT Trial
  - 18,790 patients from 26 countries, aged 50-80 with DBP 100-115 mmHg
    - 6264 patients had target DBP  $\leq$  90 mmHg
    - 6264 patients had target DBP  $\leq$  85 mmHg
    - 6262 patients had target DBP  $\leq$  80 mmHg
  - Primary outcome: fatal and non-fatal myocardial infarctions, fatal and non-fatal strokes, other cardiovascular deaths

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## Diastolic Blood Pressure – HOT Trial

Event	Number of events	Events/1000 patient-years	p for trend	Comparison	Relative risk (95% CI)
<b>Major cardiovascular events</b>					
$\leq$ 90 mm Hg	232	9.9		90 vs 85	0.99 (0.83-1.19)
$\leq$ 85 mm Hg	234	10.0		85 vs 80	1.08 (0.89-1.29)
$\leq$ 80 mm Hg	217	9.2	0.50	90 vs 80	1.07 (0.85-1.28)
<b>Major cardiovascular events, including silent myocardial infarction</b>					
$\leq$ 90 mm Hg	274	11.7		90 vs 85	0.99 (0.84-1.17)
$\leq$ 85 mm Hg	276	11.8		85 vs 80	1.05 (0.88-1.24)
$\leq$ 80 mm Hg	263	11.2	0.66	90 vs 80	1.04 (0.88-1.23)
<b>All myocardial infarction</b>					
$\leq$ 90 mm Hg	94	3.6		90 vs 85	1.02 (0.95-1.02)
$\leq$ 85 mm Hg	64	2.7		85 vs 80	1.05 (0.74-1.48)
$\leq$ 80 mm Hg	52	2.0	0.05	90 vs 80	1.07 (0.90-1.24)
<b>All myocardial infarction, including silent cases</b>					
$\leq$ 90 mm Hg	127	5.1		90 vs 85	1.19 (0.92-1.54)
$\leq$ 85 mm Hg	107	4.6		85 vs 80	1.30 (0.76-1.98)
$\leq$ 80 mm Hg	107	4.6	0.15	90 vs 80	1.19 (0.92-1.53)
<b>All stroke</b>					
$\leq$ 90 mm Hg	94	4.0		90 vs 85	0.85 (0.64-1.11)
$\leq$ 85 mm Hg	111	4.7		85 vs 80	1.24 (0.94-1.64)
$\leq$ 80 mm Hg	89	3.8	0.74	90 vs 80	1.05 (0.79-1.41)
<b>Cardiovascular mortality</b>					
$\leq$ 90 mm Hg	87	3.7		90 vs 85	0.97 (0.72-1.30)
$\leq$ 85 mm Hg	90	3.8		85 vs 80	0.92 (0.70-1.24)
$\leq$ 80 mm Hg	96	4.1	0.45	90 vs 80	0.90 (0.68-1.21)
<b>Total mortality</b>					
$\leq$ 90 mm Hg	186	7.9		90 vs 85	0.97 (0.79-1.19)
$\leq$ 85 mm Hg	184	8.2		85 vs 80	0.93 (0.77-1.14)
$\leq$ 80 mm Hg	167	6.8	0.35	90 vs 80	0.91 (0.74-1.10)

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### Recommendation 3

“In the general population younger than 60 years, initiate pharmacologic treatment to lower BP at SBP of 140 mmHg or higher and treat to a goal SBP of lower than 140 mmHg.”

*Expert Opinion – Grade E*

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### Systolic Blood Pressure

- Continue the current standard of 140 mmHg in absence of any RCTs
- Difficult to determine if benefits on outcomes were due to reductions in DBP, SBP, or both
- Similar SBP goal for other patient groups to facilitate implementation of the guidelines

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### Recommendation 4

“In the population aged 18 years or older with CKD, initiate pharmacologic treatment to lower BP at SBP of 140 mmHg or higher or DBP of 90 mmHg or higher and treat to goal SBP of lower than 140 mmHg and goal DBP lower than 90 mmHg.”

*Expert Opinion – Grade E*

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### Chronic Kidney Disease

- In population less than 70 with hypertension and chronic kidney disease:
  - Insufficient evidence if there is a benefit in cardiovascular outcomes, cerebrovascular outcomes, or mortality of treatment with antihypertensive therapy to a lower BP goal (<130/80 mmHg vs. <140/90 mmHg)
  - Moderate evidence of no benefit of treatment with antihypertensive therapy to a lower BP goal on progression of kidney disease
- In population with hypertension and proteinuria:
  - Insufficient evidence if there is a benefit in cardiovascular outcomes, cerebrovascular outcomes, or mortality of treatment with antihypertensive therapy to a lower BP goal (<130/80 mmHg vs. <140/90 mmHg)

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### Recommendation 5

“In the population aged 18 years or older with diabetes, initiate pharmacologic treatment to lower BP at SBP of 140 mmHg or higher or DBP of 90 mmHg or higher and treat to a goal SBP of lower than 140 mmHg and goal DBP lower than 90 mmHg.”

*Expert Opinion – Grade E*

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### Diabetes

- Treatment to a SBP goal of less than 150 mmHg improves cardiovascular and cerebrovascular outcomes, mortality
- UKPDS:
  - Randomized, multi-center, controlled trial that compared tight control of BP (goal < 150/85 mmHg) with less tight control (goal < 180/105 mmHg)
  - 1148 hypertensive patients with type 2 diabetes
  - Main outcomes: first clinical end point related to diabetes; death related to diabetes; death from all causes

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## Diabetes

- UKPDS Results:
  - Mean BP in tight control group was significantly lower than less tight control group (144/82 mmHg vs. 154/87 mmHg) (P<0.0001)
  - In tight control group:
    - 24% reduction in diabetes related end points (95% CI, 8-38%, P=0.0046)
    - 32% reduction in deaths related to diabetes (95% CI, 6-51%, P=0.019)
    - 44% reduction in stroke (95% CI, 11-65%, P=0.013)
    - 37% reduction in microvascular end points (95% CI, 11-56%, P=0.0092)

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## Diabetes

- Does a lower SBP goal have better outcomes?
  - SBP goal less than 130 mmHg not supported by any RCTs that met the panel's inclusion criteria
  - ACCORD-BP:
    - Compared SBP goal less than 120 mmHg with a SBP goal less than 140 mmHg
    - No difference in rate of nonfatal myocardial infarction, nonfatal stroke, cardiovascular death
    - Annual rate of stroke was 0.32% and 0.53% in the two groups (hazard ratio 0.59; 95% CI, 0.39-0.89, P=0.01)
    - Insufficient evidence to recommend SBP goal of less than 120 mmHg in adults with diabetes and hypertension

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## Diabetes

- Does a lower DBP goal have better outcomes?
  - DBP goal less than 80 mmHg not supported by any RCTs that met the panel's inclusion criteria
  - HOT Trial:
    - 1501 patients with diabetes
    - Major cardiovascular events were 106% higher in the ≤ 90 mmHg group compared to the ≤ 80 mmHg group (45 vs. 22 events; RR 2.06; 95% CI, 1.24-3.44)
      - Low quality evidence: post-hoc analysis; only 8% of the study population had diabetes

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### Recommendation 6

“In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB).”

*Moderate Recommendation – Grade B*

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### Antihypertensive Therapy

- Comparable effects on overall mortality, and cardiovascular, cerebrovascular, kidney outcomes by the four recommended drug classes
- For heart failure: thiazide-type diuretic was more effective than a CCB or ACEI, and ACEI was more effective than a CCB
- In ALLHAT, doxazosin vs. chlorthalidone
  - No significant difference for combined nonfatal MI and CHD death, all-cause mortality or combined CHD
  - Doxazosin was associated with:
    - 26% increased risk of stroke (95% CI, 1.10-1.46, P=0.001)
    - 80% increased risk of heart failure (95% CI, 1.61-2.02, P<0.001)

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### Antihypertensive Therapy

- No RCTs of good or fair quality comparing the following drug classes to the four recommended classes:
  - Dual alpha-1, beta blockers (carvedilol)
  - Cardioselective beta blockers (nebivolol)
  - Central alpha-2 agonists (clonidine)
  - Direct vasodilators (hydralazine)
  - Aldosterone receptor antagonists (spironolactone)
  - Peripheral adrenergic neuron antagonists (reserpine)
  - Loop diuretics (furosemide)
  - Nitrate-containing agents
  - Direct renin inhibitors (aliskiren)
  - Potassium-sparing diuretics as monotherapy (amiloride)

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### Losartan vs. Atenolol – LIFE Trial

- Double-blind, randomized, parallel-group trial
- 9,193 patients, 55-80 years old with essential hypertension and left ventricular hypertrophy
- Randomized to receive losartan or atenolol
- Mean follow-up was 4.8 years
- Primary outcome: composite of CV mortality, fatal and non-fatal MI, fatal and non-fatal stroke

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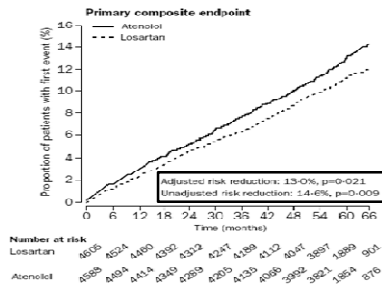
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### Losartan vs. Atenolol – LIFE Trial




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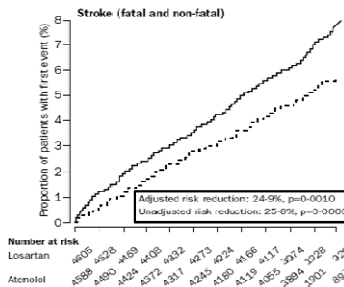
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### Losartan vs. Atenolol – LIFE Trial




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### Losartan vs. Atenolol – LIFE Trial

- Results favored losartan:
  - Relative risk reduction of 13% in primary composite outcome (P=0.021)
  - Relative risk reduction of 24.9% in stroke (P=0.001)
  - 25% lower incidence of new-onset diabetes
  - Trend for lower total mortality
  - Trend for lower non-cardiovascular mortality

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### Evidence-Based Dosing

Antihypertensive Medication	Initial Daily Dose, mg	Target Dose in ECTs Reviewed, mg	No. of Doses per Day
<b>ACE inhibitors</b>			
Captopril	50	150-200	2
Enalapril	5	20	1-2
Lisinopril	10	40	1
<b>Angiotensin receptor blockers</b>			
Eprosartan	400	600-800	1-2
Candesartan	4	12-32	1
Losartan	50	100	1-2
Valsartan	40-80	160-320	1
Irasartan	7.5	30	1
<b>β-Blockers</b>			
Atenolol	25-50	100	1
Metoprolol	50	100-200	1-2
<b>Calcium channel blockers</b>			
Amlodipine	2.5	10	1
Diltiazem sustained release	120-300	360	1
Nitrendipine	10	20	1-2
<b>Thiazide-type diuretics</b>			
Bendroflumethiazide	5	10	1
Chlorthalidone	12.5	25-50	1
Hydrochlorothiazide	12.5-25	25-100 <sup>a</sup>	1-2
Ispatamide	1.25	1.25-2.5	1

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### Recommendation 7

“In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.”

*For general black population: Moderate Recommendation – Grade B*

*For black patients with diabetes: Weak Recommendation – Grade C*

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### Black Population – ALLHAT Trial

- Randomized, double-blind, multi-centered, active-controlled clinical trial, Feb 1994 through March 2002
- 33,357 participants, 55 years or older with hypertension and at least one other CHD risk factor
  - 11,792 black patients
- Random assignment to chlorthalidone 12.5-25 mg/day, amlodipine 2.5-10 mg/day, or lisinopril 10-40 mg/day
- Primary outcome: combined fatal CHD or nonfatal MI
- Secondary outcome: all-cause mortality, stroke, combined CHD, combined CVD
- Mean follow-up was 4.9 years

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### Black Population – ALLHAT Trial

- Results:
  - For lisinopril vs. chlorthalidone
    - RR 1.40 for stroke (95% CI, 1.17-1.68)
    - RR 1.32 for heart failure (95% CI, 1.11-1.58)
    - RR 1.19 for combined CVD (95% CI, 1.09-1.30)
  - Mean follow-up systolic BP was 4 mmHg higher in the lisinopril vs. chlorthalidone group
  - Angioedema: 2 of 5369 for chlorthalidone, 23 of 3210 for lisinopril (P<0.001)

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### Black Population – ALLHAT Trial

- Pre-specified Subgroup Analysis compared use of ACEI and CCB
  - RR 1.51 of stroke in lisinopril group (95% CI 1.22-1.86)
  - For lisinopril group, average follow-up BP was 2.7/1.6 mmHg higher in men and 3.9/2.1mmHg in women
- For black patients with diabetes: outcomes not reported in eligible studies
  - Extrapolated from ALLHAT, in which 46% of black patients had diabetes

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### Recommendation 8

“In the population aged 18 years or older with CKD and hypertension, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve health outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status.”

*Moderate Recommendation – Grade B*

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### Chronic Kidney Disease

- ACEI or ARB improves kidney outcomes for patients with CKD, with and without proteinuria
- No strong evidence of improved cardiovascular outcomes with ACEI or ARB in patients with chronic kidney disease
- For black patients with CKD and proteinuria, recommended initial therapy is ACEI or ARB
- For black patients with CKD without proteinuria, recommended initial therapy is thiazide-type diuretic, CCB, ACEI, or ARB
- Monitor electrolytes (K+) and serum creatinine, and reduce dose or discontinue therapy if necessary

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### Chronic Kidney Disease – AASK Trial

- 1094 African Americans aged 18 to 70 with hypertensive renal disease
- Compared effects of 2 levels of MAP control and initial treatment with a  $\beta$ -blocker (metoprolol), an ACEI (ramipril), or a dihydropyridine CCB (amlodipine) on GFR decline
- Primary outcome: rate of change in GFR
- Secondary clinical composite outcome: confirmed reduction in GFR by 50% from baseline; ESRD; or death

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## Chronic Kidney Disease – AASK Trial

- ▣ **Results:**
  - Mean GFR slope did not differ significantly between the two BP groups (average 128/78 mmHg vs 141/85 mmHg)
  - No significant differences in GFR slope among drug groups
  - On clinical composite outcome:
    - Ramipril compared to metoprolol
      - Risk reduction of 22% (95% CI, 1-38%; P=0.04)
    - Ramipril compared to amlodipine
      - Risk reduction of 38% (95% CI, 14-56%, P=0.004)
- ▣ **Conclusion: ACEI more effective than  $\beta$ -blockers or dCCBs in slowing GFR decline**

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## Recommendation 9

- ▣ If goal BP is not achieved within one month of treatment, increase the dose of the initial drug or add a second drug from one of the recommended classes
- ▣ If goal BP cannot be reached with 2 drugs, add and titrate a third recommended drug
- ▣ If goal BP cannot be reached with recommended drugs because of a contraindication or need to use more than 3 drugs, antihypertensive drugs from other classes can be used

*Expert Opinion – Grade E*

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## Strategies for Dosing

Strategy	Description	Details
A	Start one drug, titrate to maximum dose, and then add a second drug	If goal BP is not achieved with the initial drug, titrate the dose of the initial drug up to the maximum recommended dose to achieve goal BP. If goal BP is not achieved with the use of one drug despite titration to the maximum recommended dose, add a second drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB) and titrate up to the maximum recommended dose of the second drug to achieve goal BP. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP.
B	Start one drug and then add a second drug before achieving maximum dose of the initial drug	Start with one drug then add a second drug before achieving the maximum recommended dose of the initial drug, then titrate both drugs up to the maximum recommended doses of both to achieve goal BP. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP.
C	Begin with 2 drugs at the same time, either as 2 separate pills or as a single pill combination	Initiate therapy with 2 drugs simultaneously, either as 2 separate drugs or as a single pill combination. Some committee members recommend starting therapy with 2 drugs when SBP is $\geq 160$ mm Hg and/or DBP is $\geq 100$ mm Hg, or if SBP is $\geq 24$ mm Hg above goal and/or DBP is $\geq 10$ mm Hg above goal. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose.

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### Analysis/Limitations

- Three specific questions were addressed
- Evidence review included only RCTs
- Studies from different time periods have different clinical trial designs and analytic techniques
- Recommendations only apply to those with hypertension
- In studies focused on DBP, difficult to determine if benefits were due to lowering SBP, DBP, or both
- Not designed to assess impact of therapy-associated adverse effects
- Not endorsed by any federal agency or professional society

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### Comparison of 2014 Hypertension Guidelines to Other Guidelines

- European Society of Hypertension/European Society of Cardiology 2013
  - General  $\geq$  80 years: < 150/90 mmHg
- Canadian Hypertension Education Program 2013
  - General  $\geq$  80 years: < 150/90 mmHg
- National Institute for Health and Clinical Excellence 2011
  - General  $\geq$  80 years: < 150/90 mmHg
- Kidney Disease Improving Global Outcome 2012
  - CKD + proteinuria:  $\leq$  130/80 mmHg
- American Diabetes Association 2013
  - Diabetes: < 140/80 mmHg

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### Patient Case

- What is Mr. C's goal BP?
  - A. < 150/90 mmHg
  - B. < 140/90 mmHg
  - C. < 140/80 mmHg
  - D. < 130/80 mmHg

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### Patient Case

- BP 180/84 mmHg, repeat BP 161/89 mmHg (HR 60)
- What would you recommend?
  - A. Add carvedilol 6.25 mg po bid, monitor BP& HR closely
  - B. Add spironolactone 25 mg po daily, monitor chem 8 closely
  - C. Add hctz 12.5 mg po daily, monitor chem 8 closely
  - D. Add aliskiren 150 mg po daily

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### Summary

Patient Population	Blood Pressure Goal	Recommended Initial Antihypertensive Therapy
General and < 60 years	< 140/90 mmHg	Thiazide-type diuretic, CCB, ACEI, or ARB*
General and ≥ 60 years	< 150/90 mmHg	Thiazide-type diuretic, CCB, ACEI, or ARB*
CKD and ≥ 18 years	< 140/90 mmHg	ACEI or ARB
Diabetes and ≥ 18 years	< 140/90 mmHg	Thiazide-type diuretic, CCB, ACEI, or ARB*

\*For general black population, including those with diabetes, initial antihypertensive therapy should include a thiazide-type diuretic or CCB

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